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Amendments to the claims:

Please amend the claims as indicated below. This listing of claims replaces all earlier versions of the claims in the application:

1. (Currently amended) A method for treating a degenerative joint disease, in a patient in need thereof, wherein said degenerative joint disease is selected from the group consisting of osteoarthritis, spondyloses and cartilage atrophy, wherein said method comprises~~comprising~~ administering to the patient a pharmaceutically effective amount of a compound of formula I



wherein:

A is hydrogen,

(C₁-C₈)-alkyl, (C₁-C₈)-alkanoyl, (C₁-C₈)-alkoxycarbonyl or (C₁-C₈)-alkylsulfonyl, each of which is optionally substituted one, two or three times by carboxyl, amino, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-amino, hydroxy, (C₁-C₃)-alkoxy, halogen, di-(C₁-C₄)-alkyl-amino, carbamoyl, sulfamoyl, (C₁-C₄)-alkoxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, or each of which is optionally substituted one time by (C₃-C₈)-cycloalkyl, (C₁-C₄)-alkylsulfonyl, (C₁-C₄)-alkylsulfinyl, (C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfonyl, (C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfinyl, (C₆-C₁₂)-aryloxy, (C₃-C₉)-heteroaryl or (C₃-C₉)-heteroaryloxy, and is further optionally substituted one or two times by carboxyl, amino, (C₁-C₄)-alkylamino, hydroxy, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl, (C₁-C₄)-alkyloxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, wherein the heteroaryl is optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkoxycarbonyl, (C₃-C₈)-cycloalkyl, carbamoyl, which is optionally substituted on the nitrogen by (C₁-C₆)-alkyl or (C₆-C₁₂)-aryl,

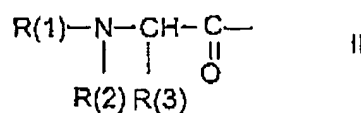
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(C₆-C₁₂)-aryl, (C₆-C₁₂)-aroyl, (C₆-C₁₂)-arylsulfonyl, (C₃-C₉)-heteroaryl or (C₃-C₉)-heteroaroyl, wherein the heteroaryl, aroyl, arylsulfonyl and heteroaroyl are each independently optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkoxycarbonyl,

or

of formula II,



wherein

R(1) is hydrogen,
(C₁-C₈)-alkyl, (C₁-C₈)-alkanoyl, (C₁-C₈)-alkoxycarbonyl or (C₁-C₈)-alkylsulfonyl, each of which is optionally substituted one, two or three times by carboxyl, amino, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-amino, hydroxy, (C₁-C₃)-alkoxy, halogen, di-(C₁-C₄)-alkyl-amino, carbamoyl, sulfamoyl, (C₁-C₄)-alkoxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, or each of which is optionally substituted one time by (C₃-C₈)-cycloalkyl, (C₁-C₄)-alkylsulfonyl, (C₁-C₄)-alkylsulfinyl, (C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfonyl, (C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfinyl, (C₆-C₁₂)-aryloxy, (C₃-C₉)-heteroaryl or (C₃-C₉)-heteroaryloxy, and is further optionally substituted one or two times by carboxyl, amino, (C₁-C₄)-alkylamino, hydroxy, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl, (C₁-C₄)-alkyloxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, wherein the heteroaryl is optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkoxycarbonyl,

(C₃-C₈)-cycloalkyl,
carbamoyl, which is optionally substituted on the nitrogen by
(C₁-C₆)-alkyl or (C₆-C₁₂)-aryl,
or
(C₆-C₁₂)-aryl, (C₆-C₁₂)-aroyl, (C₆-C₁₂)-arylsulfonyl, (C₃-C₉)-
heteroaryl or (C₃-C₉)-heteroaroyl, wherein the heteroaryl, aroyl,
arylsulfonyl and heteroaroyl are each independently optionally
substituted one, two, three or four times by carboxyl, amino,
nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-
C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl,
sulfamoyl or (C₁-C₄)-alkoxycarbonyl,

R(2) is hydrogen or methyl,

R(3) is hydrogen or (C₁-C₆)-alkyl, wherein the alkyl is optionally
monosubstituted by amino, substituted amino, hydroxy,
carbamoyl, guanidino, substituted guanidino, ureido, mercapto,
methyl-mercapto, phenyl, 4-chlorophenyl, 4-fluorophenyl, 4-
nitrophenyl, 4-methoxyphenyl, 4-hydroxyphenyl, phthalimido,
4-imidazolyl, 3-indolyl, 2-thienyl, 3-thienyl, 2-pyridyl, 3-
pyridyl or cyclohexyl, wherein the substituted amino is -NH-
A' and the substituted guanidino is -NH-C(NH)-NH-A',
wherein A' is

hydrogen,
(C₁-C₈)-alkyl, (C₁-C₈)-alkanoyl, (C₁-C₈)-
alkoxycarbonyl or (C₁-C₈)-alkylsulfonyl, each of which
is optionally substituted one, two or three times by
carboxyl, amino, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-amino,
hydroxy, (C₁-C₃)-alkoxy, halogen, di-(C₁-C₄)-alkyl-
amino, carbamoyl, sulfamoyl, (C₁-C₄)-alkoxycarbonyl,
(C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, or each of
which is optionally substituted one time by (C₃-C₈)-
cycloalkyl, (C₁-C₄)-alkylsulfonyl, (C₁-C₄)-alkylsulfinyl,
(C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfonyl, (C₆-C₁₂)-aryl-(C₁-
C₄)-alkylsulfinyl, (C₆-C₁₂)-aryloxy, (C₃-C₉)-heteroaryl

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or (C₃-C₉)-heteroaryloxy, and is further optionally substituted one or two times by carboxyl, amino, (C₁-C₄)-alkylamino, hydroxy, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl, (C₁-C₄)-alkyloxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, wherein the heteroaryl is optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkyloxycarbonyl, (C₃-C₈)-cycloalkyl, carbamoyl, which is optionally substituted on the nitrogen by (C₁-C₆)-alkyl or (C₆-C₁₂)-aryl, or (C₆-C₁₂)-aryl, (C₆-C₁₂)-aroyl, (C₆-C₁₂)-arylsulfonyl, (C₃-C₉)-heteroaryl or (C₃-C₉)-heteroaroyl, wherein the heteroaryl, aroyl, arylsulfonyl and heteroaroyl are each independently optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkyloxycarbonyl;

B is Arg, Lys, Orn, 2,4-diaminobutyroyl or L-homo-arginine, wherein the amino or the guanidino group of the side chain of Arg, Lys, Orn, 2,4-diaminobutyroyl or L-homo-arginine is independently optionally substituted by

hydrogen, (C₁-C₈)-alkyl, (C₁-C₈)-alkanoyl, (C₁-C₈)-alkyloxycarbonyl or (C₁-C₈)-alkylsulfonyl, each of which is optionally substituted one, two or three times by carboxyl, amino, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-amino, hydroxy, (C₁-C₃)-alkoxy, halogen, di-(C₁-C₄)-alkyl-amino, carbamoyl, sulfamoyl, (C₁-C₄)-alkyloxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-

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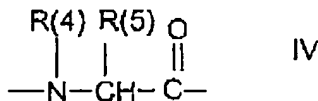
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C₃)-alkyl, or each of which is optionally substituted one time by (C₃-C₈)-cycloalkyl, (C₁-C₄)-alkylsulfonyl, (C₁-C₄)-alkylsulfinyl, (C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfonyl, (C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfinyl, (C₆-C₁₂)-aryloxy, (C₃-C₉)-heteroaryl or (C₃-C₉)-heteroaryloxy, and is further optionally substituted one or two times by carboxyl, amino, (C₁-C₄)-alkylamino, hydroxy, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl, (C₁-C₄)-alkyloxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, wherein the heteroaryl is optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkyloxycarbonyl, (C₃-C₈)-cycloalkyl, carbamoyl, which is optionally substituted on the nitrogen by (C₁-C₆)-alkyl or (C₆-C₁₂)-aryl, or (C₆-C₁₂)-aryl, (C₆-C₁₂)-aroyl, (C₆-C₁₂)-arylsulfonyl, (C₃-C₉)-heteroaryl or (C₃-C₉)-heteroaroyl, wherein the heteroaryl, aroyl, arylsulfonyl and heteroaroyl are each independently optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkyloxycarbonyl;

X is of formula IIIa or IIIb



wherein G' independently of one another is of formula IV



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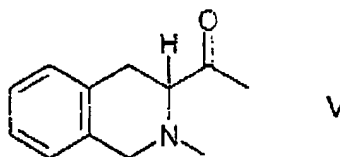
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wherein R(4) and R(5) together with the atoms they connect to form a heterocyclic mono-, bi- or tricyclic ring having 2 to 15 carbon atoms, and n is 2 to 8;

E is phenylalanine optionally substituted by halogen in the 2-, 3- or 4- ring position, tyrosine, O-methyltyrosine, 2-thienylalanine, 2-pyridylalanine or naphthylalanine;

F is covalent bond, or neutral, acidic or basic aliphatic or aromatic amino acid, which is optionally substituted in the side chain;

(D)-TIC is of formula V



G is G' or a covalent bond;

F' is covalent bond, $-\text{NH}-(\text{CH}_2)_n-$ wherein n is 2 – 8, or basic amino acid Arg or Lys in the L or D form, wherein the guanidino group or amino group of the side chain of the Arg or Lys is optionally substituted by

hydrogen,

(C₁-C₈)-alkyl, (C₁-C₈)-alkanoyl, (C₁-C₈)-alkoxycarbonyl or (C₁-C₈)-alkylsulfonyl, each of which is optionally substituted one, two or three times by carboxyl, amino, (C₁-C₄)-alkyl, (C₁-C₄)-alkyl-amino, hydroxy, (C₁-C₃)-alkoxy, halogen, di-(C₁-C₄)-alkyl-amino, carbamoyl, sulfamoyl, (C₁-C₄)-alkoxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, or each of which is optionally substituted one time by (C₃-C₈)-cycloalkyl, (C₁-C₄)-alkylsulfonyl, (C₁-C₄)-alkylsulfinyl, (C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfonyl, (C₆-C₁₂)-aryl-(C₁-C₄)-alkylsulfinyl, (C₆-C₁₂)-aryloxy, (C₃-C₉)-heteroaryl or (C₃-C₉)-heteroaryloxy, and is further optionally substituted one or two times by carboxyl, amino, (C₁-C₄)-alkylamino, hydroxy, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl, (C₁-C₄)-alkyloxycarbonyl, (C₆-C₁₂)-aryl or (C₆-C₁₂)-aryl-(C₁-C₅)-alkyl, wherein the heteroaryl is

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optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkoxycarbonyl,

(C₃-C₈)-cycloalkyl,

carbamoyl, which is optionally substituted on the nitrogen by (C₁-C₆)-alkyl or (C₆-C₁₂)-aryl,

or

(C₆-C₁₂)-aryl, (C₆-C₁₂)-aroyl, (C₆-C₁₂)-arylsulfonyl, (C₃-C₉)-heteroaryl or (C₃-C₉)heteroaroyl, wherein the heteroaryl, aroyl, arylsulfonyl and heteroaroyl are each independently optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkoxycarbonyl;

I is -OH, -NH₂ or NHC₂H₅;

K is covalent bond or -NH-(CH₂)_x-CO, wherein x is 1 to 4; and

M is covalent bond, or neutral, acidic or basic aliphatic or aromatic amino acid, which is optionally substituted in the side chain;

or its physiologically tolerable salts thereof.

2. (Original) The method according to claim 1, wherein

B is Arg, Orn or Lys,

wherein the guanidino group or the amino group of the side chain is each independently optionally substituted by (C₁-C₈)-alkanoyl, (C₆-C₁₂)-aroyl, (C₃-C₉)-heteroaroyl, (C₁-C₈)-alkylsulfonyl or (C₆-C₁₂)-arylsulfonyl, wherein the aroyl, arylsulfonyl and heteroaroyl are each independently optionally substituted one, two, three or four times by carboxyl, amino, nitro, hydroxy, cyano, (C₁-C₄)-alkylamino, (C₁-C₄)-alkyl, (C₁-C₄)-alkoxy, halogen, di-(C₁-C₄)-alkylamino, carbamoyl, sulfamoyl or (C₁-C₄)-alkoxycarbonyl;

E is phenylalanine, 2-chlorophenylalanine, 3-chloro-phenylalanine, 2-fluorophenylalanine, 3-fluorophenyl-alanine, 4-fluorophenylalanine, tyrosine, O-methyl-tyrosine or β-(2-thienyl)alanine;

K is covalent bond; and

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M is covalent bond.

3. (Original) The method according to claim 1, wherein:

A is hydrogen, (D)- or (L)-H-Arg, (D)- or (L)-H-Lys or (D)- or (L)-H-Orn;

B is Arg, Orn or Lys,

wherein the guanidino group or the amino group of the side chain is optionally substituted by hydrogen, (C₁-C₈)-alkanoyl, (C₆-C₁₂)-aroyl, (C₃-C₉)-heteroaroyl, (C₁-C₈)-alkylsulfonyl or (C₆-C₁₂)-arylsulfonyl, wherein the aroyl, arylsulfonyl and heteroaroyl are each independently optionally substituted one, two, three or four times by methyl, methoxy or halogen;

X is Pro-Pro-Gly, Hyp-Pro-Gly or Pro-Hyp-Gly;

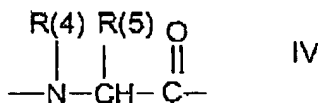
E is Phe or Thia;

F is Ser, Hser, Lys, Leu, Val, Nle, Ile or Thr;

K is covalent bond

M is covalent bond

G is of the formula IV,



wherein R(4) and R(5) together with the atoms they connect to form pyrrolidine, piperidine, tetrahydro-isoquinoline, cis- or trans-decahydroisoquinoline, cis-endo-octahydroindole, cis-exo-octahydro-indole, trans-octahydroindole, cis-endo-, cis-exo-, trans-octahydrocyclopentano[b]pyrrole, or hydroxyproline;

F' is Arg; and

I is OH.

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4. (Original) The method according to claim 1, wherein the compound of the formula I is
- H-(D)-Arg-Arg-Pro-Hyp-Gly-Thia-Ser-(D)-Tic-Oic-Arg-OH,
H-(D)-Arg-Arg-Pro-Pro-Gly-Thia-Ser-(D)-Tic-Oic-Arg-OH,
H-(D)-Arg-Arg-Pro-Hyp-Gly-Phe-Ser-(D)-Tic-Oic-Arg-OH,
H-(D)-Arg-Arg-Hyp-Pro-Gly-Phe-Ser-(D)-Tic-Oic-Arg-OH or
H-(D)-Arg-Arg-Pro-Pro-Gly-Phe-Ser-(D)-Tic-Oic-Arg-OH.
5. (Original) The method according to claim 1, wherein the compound of the formula I is D-arginyl-L-arginyl-L-prolyl-L-prolylglycyl-3-(2-thienyl)- L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(2S,3aS,7aS)-octahydro-1H-indole-2-carbonyl-L-arginine.
6. (Cancelled)
7. (Original) The method according to claim 1, wherein the administration is carried out by subcutaneous, intraarticular, intraperitoneal or intravenous injection or transdermal administration.